



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Chapter I

[Docket No. FDA-2013-N-1525]

List of Bulk Drug Substances That May Be Used in Pharmacy Compounding; Bulk Drug Substances That May Be Used to Compound Drug Products in Accordance With Section 503A of the Federal Food, Drug, and Cosmetic Act

AGENCY: Food and Drug Administration, HHS.

ACTION: Withdrawal of proposed rule; request for nominations.

SUMMARY: The Food and Drug Administration (FDA or Agency) is withdrawing the proposed rule to list bulk drug substances used in pharmacy compounding and preparing to develop a list of bulk drug substances (bulk drugs) that may be used to compound drug products, although they are neither the subject of a United States Pharmacopeia (USP) or National Formulary (NF) monograph nor components of FDA-approved drugs. To identify candidates for this bulk drugs list, interested groups and individuals may nominate specific bulk drug substances, and FDA is describing the information that should be provided to the Agency in support of each nomination.

DATES: FDA is withdrawing the proposed rule published January 7, 1999 (64 FR 996), as of [INSERT DATE OF PUBLICATION IN THE FEDERAL REGISTER].

Submit written or electronic nominations for the bulk drug substances list by [INSERT DATE 90 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: You may submit nominations, identified by Docket No. FDA-2013-N-1525, by any of the following methods.

Electronic Submissions

Submit electronic nominations in the following way:

- Federal eRulemaking Portal: <http://www.regulations.gov>. Follow the instructions for submitting “comments.”

Written Submissions

Submit written nominations in the following ways:

- Mail/Hand delivery/Courier (for paper submissions): Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Instructions: All submissions received must include the Agency name and docket number FDA-2013-N-1525 for this request for nominations. All nominations received may be posted without change to <http://www.regulations.gov>, including any personal information provided. For additional information on submitting nominations, see the “Request for Nominations” heading of the SUPPLEMENTARY INFORMATION section of this document.

Docket: For access to the docket to read background documents or nominations received, go to <http://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Marissa Chaet Brykman, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, suite 5100, Silver Spring, MD 20993-0002, 301-796-3110.

SUPPLEMENTARY INFORMATION:

I. Background

Section 503A of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 353a) describes the conditions under which a human drug product compounded for an identified individual patient based on a prescription is entitled to an exemption from three sections of the FD&C Act: (1) section 501(a)(2)(B) (21 U.S.C. 351(a)(2)(B)) (concerning current good manufacturing practice (CGMP) for drugs); (2) section 502(f)(1) (21 U.S.C. 352(f)(1)) (concerning the labeling of drugs with adequate directions for use); and (3) section 505 (21 U.S.C. 355) (concerning the approval of human drug products under new drug applications (NDAs) or abbreviated new drug applications (ANDAs)).

One of the conditions for such an exemption is that a drug product may be compounded if the licensed pharmacist or licensed physician compounds the drug product using bulk drug substances that: “(I) comply with the standards of an applicable United States Pharmacopoeia or National Formulary monograph, if a monograph exists, and the United States Pharmacopoeia chapter on pharmacy compounding; (II) if such a monograph does not exist, are drug substances that are components of drugs approved by the Secretary; or (III) if such a monograph does not exist and the drug substance is not a component of a drug approved by the Secretary, that appear on a list developed by the Secretary through regulations issued by the Secretary under subsection (d) [of Section 503A]” (section 503A(b)(1)(A)(i) of the FD&C Act).

Section 503A refers to the definition of “bulk drug substance” in FDA regulations at 21 CFR 207.3(a)(4): “any substance that is represented for use in a drug and that, when used in the manufacturing, processing, or packaging of a drug, becomes an active ingredient or a finished

dosage form of the drug, but the term does not include intermediates used in the synthesis of such substances.” See section 503A(b)(1)(A) of the FD&C Act.

Section 503A(d)(1) of the FD&C Act requires that, before issuing regulations to implement section 503A(b)(1)(A)(i)(III) of the FD&C Act, an advisory committee on compounding be convened and consulted “unless the Secretary determines that the issuance of such regulations before consultation is necessary to protect the public health” (section 503A(d)(1) of the FD&C Act).

As described in more detail below, in 1998, FDA began to develop a list of bulk drug substances that may be used in compounding, but before a final rule was published, the constitutionality of section 503A was challenged in court because it included restrictions on the advertising or promotion of the compounding of any particular drug, class of drug, or type of drug and the solicitation of prescriptions for compounded drugs. These provisions were held unconstitutional by the U.S. Supreme Court in 2002.¹ After the court decision, FDA suspended its efforts to develop the list of bulk drug substances that could be used in compounding.

The Drug Quality and Security Act (DQSA) removes from section 503A of the FD&C Act the provisions that had been held unconstitutional by the U.S. Supreme Court in 2002.² By removing these provisions, the new law removes uncertainty regarding the validity of section 503A, clarifying that it applies nationwide. Therefore, FDA is reinitiating its efforts to develop a list of bulk drug substances that may be used in compounding under section 503A.

¹ See Thompson v. Western States Med. Ctr., 535 U.S. 357 (2002).

² The DQSA also adds a new section 503B to the FD&C Act (21 U.S.C. 353b) that creates a new category of “outsourcing facilities.” For additional information concerning bulk drug substances that may be used to compound drug products in accordance with section 503B, see the notice, “Bulk Drug Substances That May Be Used to Compound Drug Products in Accordance with Section 503B of the Federal Food, Drug, and Cosmetic Act, Concerning Outsourcing Facilities; Request for Nominations” published in this issue of the Federal Register.

II. Previous Efforts to Develop the List of Bulk Drug Substances Under Section 503A of the FD&C Act

In the Federal Register of April 7, 1998 (63 FR 17011), FDA invited all interested persons to nominate bulk drug substances for inclusion on the list of bulk drug substances that may be used in compounding under section 503A. In total, FDA received nominations for 41 different drug substances. After evaluating the nominated drugs and consulting with the Pharmacy Compounding Advisory Committee as required by section 503A, FDA published a proposed rule proposing to list 20 drugs on the section 503A bulk drugs list in January 1999 (64 FR 996, January 7, 1999). The proposed rule also discussed 10 nominated drug substances that were still under consideration for the bulk drugs list. The Pharmacy Compounding Advisory Committee reconvened in May 1999 to discuss drugs included in the proposed rule, in addition to other bulk drug substances (see 64 FR 19791 (April 22, 1999)). However, as explained previously (see the “Background” section), after the 2002 U.S. Supreme Court decision, the Agency suspended its efforts to develop the bulk drugs list under section 503A.

FDA intends to reconsider the bulk drug substances that were proposed for inclusion on the list and that neither have an applicable USP or NF monograph nor are components of an FDA-approved drug due to the time lapse since the last proposal. Therefore, the Agency withdraws the proposed rule, “List of Bulk Drug Substances That May Be Used in Pharmacy Compounding,” published in the Federal Register of January 7, 1999 (64 FR 996).

III. Request for Nominations

To identify candidates for this list, FDA is seeking public input in the form of specific bulk drug nominations. All interested groups and individuals may nominate specific bulk drug substances for inclusion on the list. After evaluating the nominations and, as required by section

503A, consulting with the USP and the Pharmacy Compounding Advisory Committee, FDA will issue the list as a regulation under notice-and-comment rulemaking procedures.

Nominations should include the following information about the bulk drug substance being nominated and the product(s) that will be compounded using such substance, and any other relevant information available. If the information requested is unknown or unavailable, that fact should be noted accordingly.

Bulk Drug Substance

- Ingredient name;
- Chemical name;
- Common name(s);
- Chemical grade or description of the strength, quality, and purity of the ingredient;
- Information about how the ingredient is supplied (e.g., powder, liquid);
- Information about recognition of the substance in foreign pharmacopeias and the status of its registration(s) in other countries, including whether information has been submitted to USP for consideration of monograph development; and
- A bibliography of available safety and efficacy data,³ including any relevant peer-reviewed medical literature.

Compounded Product

- Information about the dosage form(s) into which the drug substance will be compounded (including formulations);
- Information about the strength(s) of the compounded product(s);

³ FDA recognizes that the available safety and efficacy data supporting consideration of a bulk drug substance for inclusion on the list may not be of the same type, amount, or quality as is required to support an NDA.

- Information about the anticipated route(s) of administration of the compounded product(s);
- Information about the past and proposed use(s) of the compounded product(s), including the rationale for its use or why the compounded product(s), as opposed to an FDA-approved product, is necessary; and
- Available stability data for the compounded product(s).

FDA cannot guarantee that all drugs nominated during the nomination period will be considered for inclusion on the next published bulk drugs list. Nominations received during the nomination period that are supported by the most complete and relevant information will likely be evaluated first. Nominations that are not evaluated during this first phase will receive consideration for list amendments, as the development of this list will be an ongoing process. Individuals and organizations also will be able to petition FDA to make additional list amendments after the list is published.

Interested persons may submit either electronic nominations to <http://www.regulations.gov> or written nominations to the Division of Dockets Management (see ADDRESSES). It is only necessary to send one set of nominations. Identify nominations with the docket number found in the brackets in the heading of this document. Received nominations may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at <http://www.regulations.gov>.

Dated: November 27, 2013.

Leslie Kux,

Assistant Commissioner for Policy.

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